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July 14, 2003

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-23 (Cancelled).

B/ 24. (Previously Presented) A bioreductive conjugate comprising a bioreductive moiety with at least one therapeutic agent linked thereto and physiologically acceptable derivatives thereof wherein the bioreductive moiety incorporates an aromatic ring substituted with a nitro group and the conjugate is such that bio-reduction of the nitro group causes release of the therapeutic agent by a through bond elimination and the residue of the bioreductive moiety to undergo an intramolecular cyclization reaction in which the nitrogen of the original nitro group provides an atom of the thus formed ring.

25. (Previously Presented) A conjugate as claimed in claim 24 wherein the bioreductive moiety is non-cytotoxic.

26. (Previously Presented) A conjugate as claimed in claim 24 wherein the formation of the ring occurs as a result of a self-alkylation reaction.

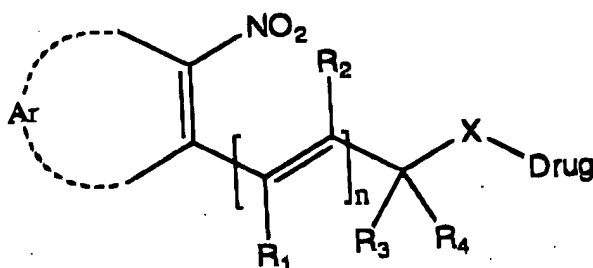
27. (Previously Presented) A conjugate as claimed in claim 24 wherein the residue of the therapeutic agent to be released on bio-reduction is bonded to the aromatic

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ring *via* a side chain attached to an atom of the aromatic ring adjacent to that to which the nitro group is bonded.

28. (Previously Presented) A conjugate as claimed in claim 24 wherein the drug moiety to be released on bioreduction is bonded to the aromatic *via* a side chain incorporating one or more double bonds which are located in the side chain between said moiety and the aromatic ring, which is/are conjugated to the aromatic ring, and which is/are displaceable to provide for elimination of moiety and formation of an arrangement of double bonds such that the residue of the bioreductive moiety is capable of undergoing the intramolecular cyclisation reaction.

29. (Currently Amended) A conjugate as claimed in claim 28 which is of the general formula (I)



in which

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the dashed lines represent completion of a substituted or unsubstituted aromatic ring system;

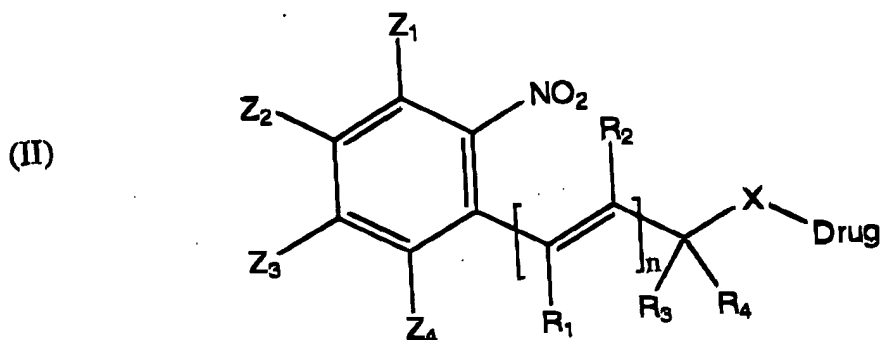
Drug is a therapeutic agent;

X is a linker (which may be part of the drug) and may for example be O, -NH, S, an amide, alcohol, phenol, carboxylic acid (carboxylate), carbonate, phosphate, sulphate or sulphonate;

R₁, R₂, R₃ and R₄ are independently hydrogen, substituted or unsubstituted alkyl [(e.g. C₁₋₄)], aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, or phosphonate; and

n is 1 to 3.

30. (Currently Amended) A conjugate as claimed in claim 29 which is of the general formula (II)

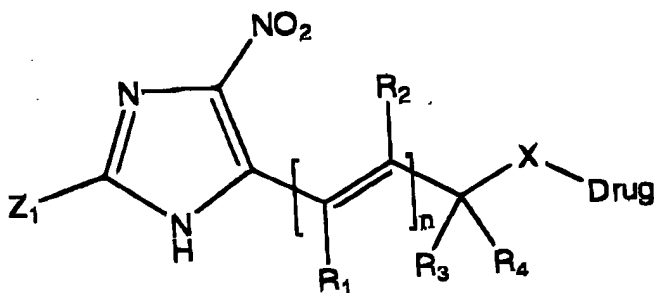


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wherein Z, Z₂, Z₃ and Z₄ are independently hydrogen, substituted or unsubstituted alkyl, aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, or phosphonate.

31. (Withdrawn) A conjugate as claimed in claim 29 which is of the general formula (III)


(III)



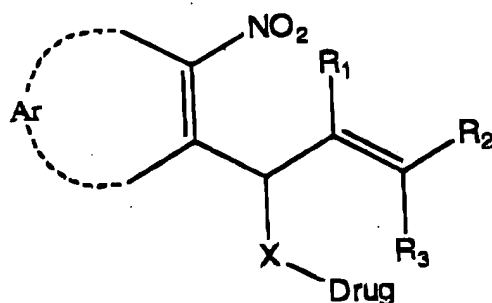
32. (Previously Presented) A conjugate as claimed in claim 29 wherein n=1.

33. (Withdrawn) A conjugate as claimed in claim 24 wherein the drug moiety to be released on bioreduction is bonded to the carbon atom adjacent to the aromatic ring of a side chain bonded to that ring and that carbon atom is bonded to an olefinic double bond of the side chain.

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34. (Withdrawn) A conjugate as claimed in claim 33 which is of the formula

(IV)



(IV)

in which

Drug and X are as defined above;

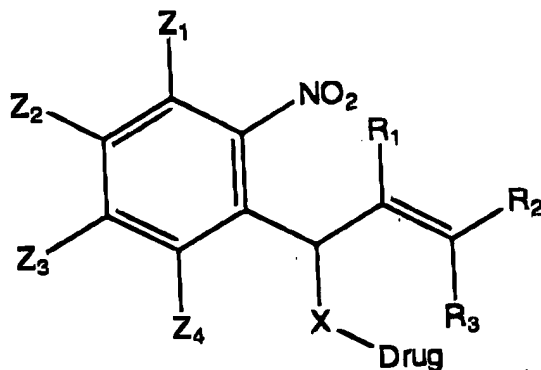
the dashed lines represent completion of a substituted or unsubstituted aromatic ring; and

R₁, R₂ and R₃ are independently hydrogen, substituted or unsubstituted alkyl (e.g. C₁₋₄), aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, phosphonate.

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35. (Withdrawn) A conjugate as claimed in claim 34 which is of the formula

(V)

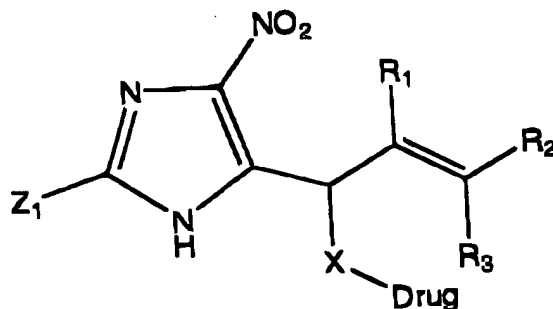


(V)

Bl
amt

36. (Withdrawn) A conjugate as claimed in claim 34 which is of the formula

(VI)



(VI)

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37. (Currently Amended) A conjugate as claimed in claim 24 wherein the therapeutic agent is an anti-infective, ~~such as an antibiotic or antiviral agents~~, analgesic, anaesthetic, anti-inflammatory or anti-neoplastic agent.

38. A therapeutic composition comprising a bioreductive conjugate as claimed in claim 24 in conjunction with a therapeutically acceptable carrier.

B/cmt 39. (Cancelled). ✓

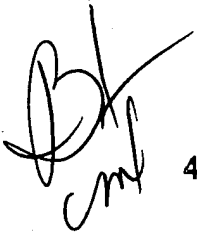
40. (Currently Amended) ~~The A method as claimed in claim 39~~ of therapeutic treatment, wherein the therapeutic treatment is for the treatment of a condition associated with hypoxia and/or ischemia, comprising administering to a subject in need thereof a therapeutically effective amount of a bioreductive conjugate as claimed in claim 24.

41. (Currently Amended) ~~The A method as claimed in claim 39~~ of therapeutic treatment, wherein the therapeutic treatment is for the treatment of an inflammatory condition, diabetes, atherosclerosis, stroke, sepsis, Alzheimer's disease and other neurological diseases, cancer, kidney disease, digestive diseases, liver disease, chronic periodontitis and ischemia following tissue transplantation, comprising administering to a

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subject in need thereof a therapeutically effective amount of a bioreductive conjugate as claimed in claim 24.

42. (Currently Amended) The method as claimed in the claim 41 when the therapeutic treatment is for the treatment of rheumatoid arthritis or other arthritic condition [[such as oosteoarthritis]].



43. (Previously Presented) The method as claimed in claim 41 wherein the therapeutic treatment is for the treatment of an inflammatory condition of soft tissue.


44. (Currently Amended) The method as claimed in claim 42 wherein the therapeutic treatment is for the treatment of a gastrointestinal disorder[[, for example, Crohn's disease]].

45. (Previously Presented) The method as claimed in claim 43 wherein the therapeutic treatment is for use in the healing of wounds (acute and chronic), and the treatment of fibrotic disorders, ulcerative colitis, inflammatory bowel disease, epilepsy, cardiovascular reperfusion injury, cerebral reperfusion injury, hypertension, cystic

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fibrosis, psoriasis, para-psoriasis, peptic ulcers, gastric ulcers, duodenal ulcers, diabetic ulcers, dementia, oncology and AIDS.

46. (New) The conjugate according to claim 29 wherein R_1 , R_2 , R_3 and R_4 are independently hydrogen, substituted or unsubstituted C_{1-4} alkyl, aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, or phosphonate.

 47. (New) The conjugate according to claim 30 wherein Z_1 , Z_2 , Z_3 and Z_4 are independently hydrogen, substituted or unsubstituted C_{1-4} alkyl, aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, or phosphonate.

48. (New) The conjugate according to claim 37 wherein the anti-infective agent is an antibiotic or antiviral agent.

49. (New) The method according to claim 42 wherein said other arthritic condition is osteoarthritis.

50. (New) The method according to claim 44 wherein said gastrointestinal disorder is Crohn's disease.